

## **Technical abstract**

Small Cell Lung Cancer (SCLC) represents one fourth of the 150,000 lung cancers that occur each year in the United States. Despite a high initial chemosensitivity, most of these cancers ultimately relapse. Once relapse has occurred, then the chance of responding to additional conventional chemotherapy is unusual. There has been increasing interest in recent years in developing immunologic approaches to malignancies, and there is some evidence that the growth of SCLC can be modulated by the host's immune system. One therapeutic approach that is being investigated by several groups is to over express B7-1 to enhance the immunogenicity of tumors. In order to mount a cytotoxic response, T cells need two signals: the binding of the T cell receptor (TCR) to the antigen presented on MHC molecules of antigen presenting cells (APC's), and the binding of CD28 to B7-1 on APC's. B7-1 is expressed by APC's but not by SCLC cells. It has been shown that in mice tolerant to a tumor, the implantation of tumor cells transfected with B7-1 can induce regression of the primary tumor. An additional characteristic of SCLC cells is that they are deficient in antigen presentation. This defect can be restored by interferon gamma stimulation.

Patients enrolled on this protocol will be treated with a combination of systemic interferon gamma and autologous tumor cells modified to express B7-1 which will function as a tumor vaccine. Specifically, tumor cells will be taken from the patient at diagnosis and adapted to *in vitro* culture. The patient will receive standard chemotherapy. The cultured tumor cells will then be transfected with an expression vector containing the human B7-1 gene. When relapse occurs, or in case of partial remission not amenable to irradiation in patients with extensive disease, tumor cells will be

treated with interferon gamma, irradiated and injected subcutaneously into the patients at 2 week intervals. Interferon gamma will then be given to the patients systemically on the second week after vaccine injection, allowing for priming of the immune response by the vaccine during the first week. Clinical response will be assessed in a planned accrual of 30 patients, as well as the kinetics of a cytotoxic response in vitro.